PATENT
Docket No. 13761-7064

IN THE U[redacted]TED STATES PATENT AND TRADEMARK OFFICE

Applicants:	DeLeve[redacted]aurie	Confirmation No.:	1401
Filing Date:	Februa[redacted]7, 2002	Examiner:	Sharareh, Shahnam J.
Serial No.:	10/086,[redacted]2	Group Art Unit:	1617
Title:	**COMPO[redacted]TION AND METHOD FOR PREVENTING AND TREATING SINUSO[redacted]AL OBSTRUCTION SYNDROME AND RADIATION-INDUCED LIVER [redacted]EASE**		

Commissioner for Pa[redacted]ts
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DECLAR[redacted]ION OF LAURIE DELEVE UNDER 37 C.F.R. § 1.132

I, Laurie DeLeve, citi[redacted] of the United States, hereby declare that:

1. I am the Lauri[redacted]eLeve who is the named inventor of the above-identified application. I also ar[redacted]he Laurie DeLeve who is the first author of the attached publication entitled "S[redacted]usoidal Obstruction Syndrome (Veno-Occlusive Disease) in the Rat is Prevented by [redacted]trix Metalloproteinase Inhibition", Gastroenterology (2003) **125**:882-890. All stu[redacted]s reported in this publication were performed by me or under my direction and supervi[redacted]n.

2. The attached [redacted]blication reports on Applicant's discovery that sinusoidal obstruction syndrom[redacted]SOS) is caused by up-regulation of metalloproteinase enzyme in a clinically relevant a[redacted]nal model of the disease. Applicant also reports that inhibition of matrix metalloprotein[redacted]e-9 and metalloproteinase-2 activity matrix (MMP-9 and MMP-2,

respectively) activity [redacted] administration of effective amounts of metal metalloproteinase inhibitors prevented t[redacted] development of SOS in this animal model.

3. As noted on p[redacted]e 884 of the publication, 2 different MMP inhibitors were administered to the a[redacted]nals. One subgroup received 3 different doses of doxycycline (5, 10 and 15 mg/kg [redacted]) twice daily from day -2 until the time of sacrifice. The second group received the M[redacted]P-2/MMP-9 inhibitor 2-[4-biphenylsulfonyl)amino]-3-phenyl-propionic acid at two[redacted]fferent doses, namely 100 or 200 µg/hour. The drug was infused intraportally using ar[redacted]iniosmotic pump via a cannula inserted into the inferior mesenteric vein fror[redacted]ay -1 until the time of sacrifice. Control studies were performed with 2 chemically m[redacted]fied tetracyclines that are known weak MMP inhibitors: isochloro- and anhydrotetracyc[redacted]e, 15 mg/kg IG, were given twice daily from day -2 on.

5. On page 887 [redacted] the publication, it is reported that clinical signs of SOS in this model, e.g., ascites [redacted]rmation, increased liver weight, and decreased hematocrit, were completely preventeby 2-[4-biphenylsulfonyl)amino]-3-phenyl-propionic acid, and were nearly completely p[redacted]ented by 15 mg/kg IG of doxycycline. What is inferred, but not explicitly stated in th[redacted] publication is that lower dosages (5 and 10 mg/kg) did not prevent clinical sign[redacted]f SOS in the animals.

6. I further decl[redacted] that all statements made herein of my own knowledge are true and all statements [redacted]de on information and belief are believed to be true; and further that these statemen[redacted] were made with the knowledge that willful false statements and the like so made ar[redacted]unishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the Unite[redacted]States Code and that such willful false statements may jeopardize the validity of the a[redacted]ication or any patent issued thereon.

Date: May 26, 200[redacted]

Laurie DeLeve, M.D.

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